D1 cont'd SEQ ID NO: 1.

B2 cont'd 2. (Amended) The polypeptide of claim 1 wherein the portion of CFTR protein comprises 22 amino acid residues as shown in SEQ ID NO: 2.

B2 D1 cont'd 7. (Amended) The polypeptide of claim 1, wherein the portion of CFTR protein consists of a sequence of amino acid residues as shown in SEQ ID NO: 2, and wherein the portion is free of phosphorylation.

IN THE SPECIFICATION

B3 The paragraph at page 8, lines 5-14.

It is believed that the administration of the polypeptide of the present invention will be the most useful in treatment of a class of mutants which produce CFTR proteins which are properly delivered to the plasma membrane but which are only residually or minimally active. Known mutants of CFTR are listed at the following URL address: http file type, www host server, domain name genet.sickkids.on.ca, directory cftr-cgi-bin, subdirectory fulltable. One can determine that a particular CFTR mutant is fully processed and reaches the plasma membrane in a Western blot assay using antibody against CFTR. Fully processed mutants achieve mature glycosylation status and appear on the gel as "band C and band B" whereas mutants that are retained in the endoplasmic reticulum are not fully glycosylated and show only "band B". See Example 2, below and Figure 1C.

The paragraph at beginning at page 9, line 18 and ending at page 10, line 12.

B4 The R domain of CFTR contains two negatively charged regions, amino acids 725-733 (NEG1) and amino acids 817-838 (NEG2), that reside in close proximity to two PKA

phosphorylation sites, S737 and S813, used in vivo (Figure 1A) (Cheng, et al. 1991). NEG2 is predicted to form an amphipathic (-helical structure with a negatively charged face (Figure 1B) (Geourjon and Deleage, 1995, Rost and Sander, 1993, Rost and Sander, 1994). Three mutations (E822K, E826K, D836Y), two of which were clearly obtained from patients with CF (E822K and D836Y), have been identified within the NEG2 region that result in the removal of negative charges (See URL address: www host server at domain name genet.sickkids.on.ca). The E822K CFTR channel has a low open probability relative to wt-CFTR (wild type-CFTR), but the E826K CFTR channel has single channel properties similar to wt-CFTR (Vankeerberghen et al., 1998). The presence of these disease-causing mutations suggests the potential importance of the NEG2 region. To investigate the roles of NEG1 and NEG2 in CFTR function, these regions were deleted from CFTR using mutagenesis and subcloning. The ΔNEG1- and ΔNEG2-CFTR proteins were transiently expressed in human embryonic kidney 293 cells. Membrane vesicles containing the CFTR proteins were isolated and subjected to SDS-PAGE. Like wt-CFTR, both ΔNEG1- and ΔNEG2-CFTR are present both in the core glycosylated (band B) and the fully glycosylated form (band C) (Figure 1C).

REMARKS

The Amendments

Claim 1 has been amended to recite a lower limit of 18 rather than 10 amino acid residues in the portion of CFTR protein. The amendment to claim 1 is supported by the specification which discloses that the isolated polypeptide comprises a portion of CFTR protein that "preferably contains at least 18 amino acids as shown in SEQ ID NO: 1." (Page 6, lines 18-19.)